REMARKS

The office action of October 4, 2010 has been reviewed and its contents carefully noted. Reconsideration of this case, as amended, is requested. Claim 1 remains in this case. Claims 2-6 are cancelled.

Claim 1 was amended to clarify the subject matter being claimed. Support for the amendment is found for example on page 12, lines 2-3. No new matter has been added.

A supplemental IDS is submitted with this response. The supplemental IDS contains an office action issued on January 26, 2011 by the Japanese Patent Office, three non-patent literature documents, and three patents. The non-patent literature documents and one of the two patents are discussed below.

The numbered paragraphs below correspond to the numbered paragraphs in the Office Action.

Rejection under 35 U.S.C. §112

3a. Claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Applicant has amended claim 1 to distinctly claim the protease inhibitor by claiming structural characteristics associated with the protein, such as the active site of the protein. Applicant believes that these amendments have fully addressed the Examiner's rejections, and the claim is now in condition for allowance. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §102

4a. Claim 1 was rejected under 35 U.S.C. 102(b) as being anticipated by Farina et al. (2001).

Applicant respectfully disagrees with the rejection.

Farina et al. discloses that thioredoxin, a redox enzyme with a highly conserved Cys-Gly-Pro-Cys active site when combined with flavoenzyme thioredoxin reductase (TrxR) and NADPH acts as an efficient protein disulfide reductase. Within the study conducted by Farina et al. it was found that thioredoxin inhibited activity of MMP-2, but not MMP-9 (see abstract and page 410, right col. 2nd paragraph, lines 18-21) and that differential capacity of thioredoxin to inhibit MMP-2, but not MMP-9 activity suggests a greater functional dependence of MMP-2 activity upon surface-located disulfide bonds (see page 411, left col. last line to right col. Lines 1-3).

Farina et al. does not disclose, teach, suggest the use of MMP-1, nor does the Examiner provide any support or evidence that MMP-2 would have the same protease activity and/or function, or that MMP-2 is a substitute for MMP-1. Additionally, Farina et al. teaches away from an inhibitor of MMP-9.

Furthermore, Applicant's claim 1 requires MMP-1, *not* MMP-2. MMP-1 and MMP-2 are different even though they are in the same family of matrix metalloproteinases. MMP-2 plays a primary role in the production of phlegm, is a gelatinase, and has different inhibitory effects in comparison to MMP-1. MMP-1 plays a role in remodeling and repair of tissue and is a collagenase. Furthermore, MMP-1 and MMP-9 discussed in claim 1, play an important role in remodeling and repair of tissue, whereas MMP-2 plays a role in phlegm production. As further discussed below, MMP-1 has different substrate specificity, function, and inhibitory effects from MMP-2.

As stated in Joos et al. (see IDS enclosed with this response), "MMP-1 (interstitial collagenase), MMP-9 (gelatinase B) and MMP12 (macrophage elastase) are thought to be important in the development of emphysema....Matrix metalloproteinases (MMPs) comprise a structurally and functionally related family of at least 20 proteolytic enzymes that play an essential role in tissue remodeling and repair associated with development and inflammation." (Abstract lines 1-3; page 569, left col. lines 17-20)

As stated in Imai et al. (see IDS enclosed with this response), "Immunohistochemistry studies localized MMP-1 to the Type II pneumocyte in patients with emphysema and not normal control subjects or smokers without emphysema. This observation demonstrates that the lung is altered in emphysema such that the Type II pneumocyte secretes MMP-1 and suggests that

MMP-1 may be an important enzyme involved in the destruction of the lung in the human disease....We know that constant expression of MMP-l in the lung is detrimental to the lung structure." (page 786. left col. lines 14 to 20; and page 790 left col. lines 15 to 16). Therefore Imai et al teaches that MMP-1 is an important enzyme related to destruction of human lungs in the disease.

A person skilled in the art knows that MMP-l and MMP-9 play an important role in remodeling and repair of tissue. Thus, the role of MMP-l is quite different from that of MMP-2 which plays a primary role in producing phlegm.

Furthermore, from the viewpoint where chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation throughout airways, paremchyma, and pulmonary vasculature (Lappalainen et al. – see enclosed IDS –page 311, left. col. lines 32 to 33), if MMP-l is plays an important role in remodeling tissue and MMP-1 is inhibited, it is rational that MMP-l could have the same effect on MMP-9 rather than MMP-2. Farina et al. teaches this in the fact that thioredoxin inhibited MMP-2 activity, but not MMP-9 activity.

Further, in Richards et al. (WO 01/62261 – see enclosed IDS) there is disclosed "Table I (MMP-l Lung Tissue Study) shows with 10-4 dox the value of %of control is 24.5. This means with 10-4 dox MMP-l was inhibited by about 76% compared to the control. Table II (MMP-2 Lung Tissue Study) shows with 10-4 dox the value of % of control is 33.34. This means with 10-4 dox MMP-l was inhibited by about 66% compared to the control." (Page 9 see tables 1 & 2 page 10 lines 16 to 20). That is, Richards et al. discloses the fact that doxycycline, a protease inhibitor used in the study of Richards et al., has more superior inhibitory effect against MMP-1 than against MMP-2. Again, this supports the fact that MMP-2 has a different substrate specificity from MMP-1.

While MMP-1 and MMP-2 are in the same family, they are different in function, substrate specificity, and inhibitory effects and are therefore not equivalents each other.

Therefore, it is respectfully suggested that the rejection of independent claim 1 as being anticipated by Farina et al. is overcome. Reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

Applicant believes the claims, as amended, are patentable over the prior art, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicants' attorney would advance the prosecution of the case to finality, he is invited to telephone the undersigned at the number given below.

"Recognizing that Internet communications are not secured, I hereby authorize the PTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file."

Respectfully Submitted:
Tomoaki Hoshino

By: /Lynda Wood, Reg.#53791/
Lynda Wood, Reg. No. 53,791
Agent for Applicant

BROWN & MICHAELS, P.C.
400 M&T Bank Building - 118 N. Tioga St.
Ithaca, NY 14850
(607) 256-2000 • (607) 256-3628 (fax)
e-mail: docket@bpmlegal.com
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